

A32040 PCT USA-A - 072876.0102

PATENT

IN THE CLAIMS:

Amendments to the claims are reflected in the listing of the claims.

Claim 1. (Currently Amended) A neuronal cell line obtained from a transgenic rat which expresses a SV40tsA58 gene, the cells of which comprise:

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell type specific promoter,

in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is the [a] SV40tsA58 gene

and in which the cell type specific promoter is a human NF-L gene promoter.

Claims 2-6. (Cancelled)

7. (Previously amended) A neuronal cell line obtained from a transgenic rat, the cells of which comprise:

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell type specific promoter

in which the conditional oncogene, transforming gene, immortalizing gene or the cell cycle affecting gene is a C Erb β 2 gene or a TGF α gene and in which the cell type specific promoter is a human NF-L gene promoter.

A32040 PCT USA-A - 072876.0102

PATENT

Claim 8. Cancelled.

Claim 9. (Previously amended) A cell line as claimed in claim 1 having the ECACC Accession number 96092454.

Claims 10-12. Cancelled.

Claim 13. (Currently Amended) A method of producing a transgenic rat expressing a SV40tsA58 gene, comprising:

(i) causing a female rat to super-ovulate by supplying her with a regular supply of Follicle Stimulating Hormone (FSH) prior to mating;

(ii) mating or artificially inseminating the female rat;

(iii) obtaining the resulting embryo from the female rat; and

(iv) incorporating

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell specific promoter into the genome of the rat embryo in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is said [a] SV40tsA58 gene, [C Erb β 2 gene or a TGF α gene]

and in which the cell type specific promoter is a human NF-L gene promoter.

Claim 14. Cancelled.

Claim 15. (Previously amended) A method as claimed in claim 13 wherein the FSH is supplied continuously.

A32040 PCT USA-A - 072876.0102

PATENT

16. (Previously amended) A method as claimed in claims 13 or 15 wherein the supply of FSH is from 2mg to 8mg and the FSH is supplied over a 1 to 4 day period.

17. (Currently amended) A transgenic rat which expresses a SV40tsA58 gene whose germ cells and somatic cells contain

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell type specific promoter as a result of chromosomal incorporation into the rat genome or into the genome of an ancestor of said rat

in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is [a] the SV40tsA58 gene

and in which the cell type specific promoter is a human NF-L gene promoter.

18. (Previously amended) A transgenic rat whose germ cells and somatic cells contain

(i) a conditional oncogene, transforming gene or immortalising gene or a cell cycle affecting gene operably linked to

(ii) a cell type specific promoter as a result of chromosomal incorporation into the rat genome or into the genome of an ancestor of said rat,

wherein the conditional oncogene, transforming gene, immortalising gene, or the cell cycle affecting gene is a C Erb β 2 gene or a TGF α gene,

and wherein the cell type specific promoter is a human NF-L gene

A32040 PCT USA-A - 072876.0102

PATENT

promoter.

19. (Previously amended) A method of testing a material suspected of being a carcinogen, said method comprising subjecting a rat according to claim 17 or 18 to said material and detecting neoplasms as an indication of carcinogenicity.

20. (Previously amended) A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising administering said material to a rat according to claim 17 or 18 and detecting a reduced incidence of development of neoplasms, compared to an untreated rat, as an indication of said protection.

21. (Previously amended) A method of obtaining a cell line comprising culturing a somatic cell obtained from a transgenic rat as claimed in claim 17 or 18 or an ancestor thereof.

22. (Previously amended) A cell derived from a cell line obtained from a transgenic rat as claimed in claim 17 or 18 or ancestor thereof.

23. (Previously amended) A method of obtaining a transgenic tissue comprising culturing a somatic cell obtained from a transgenic rat as claimed in claim 17 or 18 or ancestor thereof.

24. (Previously amended) A tissue derived from a somatic cell obtained from a transgenic rat as claimed in claim 17 or 18 or ancestor thereof.

25. (Currently amended) A method of generating a cell line from a transgenic rat comprising a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to a cell specific promoter wherein the

A32040 PCT USA-A - 072876.0102

PATENT

cell type specific promoter is a human NF-L gene promoter, the method comprising:

- (i) maintaining the rat at restrictive conditions such that the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a SV40tsA58 gene [, a C Erb β 2 gene, or a TGF α gene] and is expressed in vivo, only in a tissue of interest and in an inactive form such that the cells thereof grow normally;
- (ii) culturing said cells from the tissue of interest in vitro under permissive conditions such that the immortalizing function is activated; and
- (iii) subjecting the cells to non-permissive conditions so as to result in a cessation of growth and in differentiation.

26. (Original) A method as claimed in claim 25 wherein the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a temperature sensitive gene.

27. (Original) A method as claimed in claim 25 or 26 wherein the permissive condition is a temperature of 33° C and the restrictive condition is a temperature of 39° C.

28. (Original) A method of testing a material suspected of being a carcinogen, said method comprising administering said material to a rat produced according to the method of claim 16 or an ancestor thereof and detecting neoplasms as an indication of carcinogenicity.

29. (Previously amended) A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising

A32040 PCT USA-A - 072876.0102

PATENT

administering said material to a rat produced according to the method of claim 13 or an ancestor thereof and detecting a reduced incidence of development or neoplasms, compared to an untreated rat, as an indication of said protection.

30. cancelled

31. cancelled

32. cancelled

33. (Newly Added) A method of producing a transgenic rat which expresses a C Erb β 2 gene or a TGF α gene, comprising:

(i) causing a female rat to super-ovulate by supplying her with a regular supply of Follicle Stimulating Hormone (FSH) prior to mating;

(ii) mating or artificially inseminating the female rat;

(iii) obtaining the resulting embryo from the female rat; and

(iv) incorporating

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell specific promoter into the genome of the rat embryo

in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is the C Erb β 2 gene or the TGF α gene and in which the cell type specific promoter is a human NF-L gene promoter.

34. (Newly added) A method of generating a cell line from a transgenic rat comprising a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to a cell specific promoter wherein the

A32040 PCT USA-A - 072876.0102

PATENT

cell type specific promoter is a human NF-L gene promoter, the method comprising:

- (i) maintaining the rat at restrictive conditions such that the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a C Erb β 2 gene or a TGF α gene and is expressed in vivo, only in a tissue of interest and in an inactive form such that the cells thereof grow normally;
- (ii) culturing said cells from the tissue of interest in vitro under permissive conditions such that the immortalizing function is activated; and
- (iii) subjecting the cells to non-permissive conditions so as to result in a cessation of growth and in differentiation.